

17095CIPCON (AP)



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Garst)
)
Serial No.: 09/903,954)
Conf. No.: 3028)
Filed: July 12, 2001)
For: COMBINATIONS OF)
PROSTAGLANDINS AND)
BRIMONIDINE OR DERIVATIVES)
)
Group Art Unit: 1614)
)
Examiner: Fay, Z.)
_____)

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APPEAL BRIEF

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REAL PARTY IN INTEREST

The sole inventor, Michael E. Garst, assigned his entire interest in this patent application to Allergan Sales, Inc. via an assignment document recorded at reel 011717, frame 0317 and executed on November 15, 1999. Allergan Sales, Inc. was subsequently merged with Allergan Sales, L.L.C. Allergan Sales, L.L.C. then assigned its entire interest in this application to Allergan, Inc.

Allergan, Inc., is therefore the owner of this patent application and the real party in interest in this appeal.

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SUBSTITUTE APPEAL BRIEF
A-05009 CIPCON

RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

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STATUS OF CLAIMS

Claims 1 – 20 and 26 have been cancelled without prejudice.

Claims 21-25 and 27 are pending, have been rejected, and are under appeal.

STATUS OF AMENDMENTS

An amendment of claims 21 and 24 pursuant to 37 CFR §41.33 was filed on July 7, 2006 after the filing of a Notice of Appeal. These amendments were made solely in order to simplify the claims and place them in better condition for consideration on appeal. Applicants have not yet received confirmation that this amendment was entered in the present application.

No other amendments have been made since the mailing date of the Final Office Action on November 2, 2005.

The Claims Appendix of this Appeal Brief lists the claims as they appeared prior to the 37 CFR §41.33 Amendment filed July 7, 2006.

SUMMARY OF CLAIMED SUBJECT MATTER

The present application contains a single independent claim, claim 21.

Claim 21 is drawn to a method of treating degeneration of the optic nerve of a mammal in need of such treatment comprising administering to the mammal a therapeutically effective amount of a prostaglandin and a therapeutic amount of an alpha adrenergic receptor agonist of a given structure. Support for this claim can be found on e.g., page 5, lines 25-32 and pages 8 and 9 of the specification. The words “and retinal ganglion cells” were deleted from the preamble of this claim in a Rule 41.33 Amendment filed July 7, 2006; while the Claims Appendix lists the claims as they stand before entry of this Amendment, Applicants have argued the patentability of the claims on the basis of the entry of this Amendment.

Claim 22 is a dependent claim in which the prostaglandin is selected from a Markush group of specific compounds. Beyond the listed support for claim 21, support for this Markush group is found, e.g., on pages 12 and 13 of the specification.

Claim 23 is a dependent claim in which the prostaglandin is selected from a Markush group of specific compounds. Beyond the listed support for claim 21, support for this Markush group is found, e.g., on pages 12 and 13 of the specification.

Claim 25 depends from claim 14 in which the alpha adrenergic agent is brimonidine (5-bromo-N-(4,5-dihydro-1H-imidazol-2-yl)-6-quinoxalinamine). Beyond the listed support for claim 21, support for this amendment can be found e.g., on page 13, lines 6-20. Because claim 14 is a cancelled claim, Applicants changed the dependency of this claim by replacing “14” with “23” in a Rule 41.33 Amendment filed July 7, 2006. While the Claims Appendix lists the claims as they stand before entry of this Amendment, Applicants have argued the patentability of the claims on the basis of this Amendment.

Claim 27 depends from claim 21 in which the prostaglandin is the 11-pivalyl ester of PGF2 α and the alpha adrenergic agent is brimonidine. Beyond the listed support for claim 21, support for this amendment is found in originally filed claim 13.

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GROUND OF REJECTION TO BE REVIEWED ON APPEAL

Claims 21-25 and 27, all the currently pending claims, have been rejected as allegedly *prima facie* obvious over Yavitz, E., OCULAR SURG. NEWS 17:28 (September 1999) and Woodward (US Patent 5,877,211).

ARGUMENT

I. CLAIM 21

- a. Did the Examiner err in holding that Claim 21 is *prima facie* obvious over the combination of Yavitz, E., OCULAR SURG. NEWS 17:28 (September 1999) (hereinafter “Yavitz”) and Woodward (U.S. Patent 5,877,211) (hereinafter “Woodward”)?

- i. ***The Examiner has not met the burden of establishing a prima facie conclusion of obviousness, because nothing in the combination of the Yavitz and Woodward references motivates or suggests to one of ordinary skill in the art to combine an alpha adrenergic agonist and a prostaglandin for the currently claimed purpose for the treatment of degeneration of the optic nerve.***

Claim 21 has been amended in a Rule 41.33 Amendment to delete the words “and the retinal ganglion cells” from method claim 21. While the Claims Appendix shows claim 21 in its unamended state, Applicants have argued the patentability of this and dependent claims as a method for the treatment of degeneration of the optic nerve.

In order to establish a proper conclusion of *prima facie* obviousness, the burden is on the patent examiner to establish that the cited references 1) suggest or provide motivation to the person of ordinary skill in the art to combine reference teachings, 2) provide a reasonable expectation of success to such as person in making the claimed invention, and 3) teach or suggest all the claim limitations, either alone or when combined. See e.g., MANUAL OF PATENT EXAMINING PROCEDURE §2142 at 2100-134 (8th Ed., Rev. 4, 2006) (hereinafter “MPEP”); see also *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). The Applicants respectfully submit that the Examiner has not met this burden in the present case.

The invention of Claim 21 is drawn to a method for the treatment of degeneration of the optic nerve by administration to a mammal in need thereof of an alpha adrenergic agonist of a given generic structure and a prostaglandin.

Yavitz describes the results of a small study (20 patients) in which thinning of the retinal nerve fiber layer was seen in almost all patients undergoing laser in situ keratomileusis (LASIK). The hypothesis set forth in the reference is that nerve damage is due either to hypoxia (oxygen starvation) or apoptosis due to a crush injury, possibly a

mechanical injury caused by elevated intraocular pressure (IOP), transiently required during LASIK. See *Yavitz* at 28, col. 1, ¶ 3. These effects were reported to be mitigated or prevented by administration of brimonidine for one week preop and for 4 weeks postop. The author concludes that the data implies that brimonidine may be neuroprotective. *Id.* at col. 3, ¶ 4.

Woodward discusses the ability of certain agonists of the prostaglandin EP2 receptor to protect cultured rat hippocampal neurons in cell culture against challenge with the excitatory amino acids glutamate, α -amino-3-hydroxy-5-methyl-4-isoxazole proPionic acid (AMPA), N-methyl-D-aspartate (NMDA), or kainic acid. Interestingly, Woodward states “[i]t is noted that PGF2 α and PGF2 α 1-OH are inactive [in this assay], thereby indicating that this [protective result] is a specific EP2 receptor mediated effect.” U.S. Patent No. 5,877,211 (the ‘211 patent), column 8, lines 49-51 (emphasis added). Woodward notes that this effect is independent of the ability of an EP2 receptor agonist to lower IOP, since PGF2 α is said to be a potent hypotensive despite its inactivity in the neuroprotection experiments described in the Examples of the Woodward patent. See *id.* at paragraph bridging columns 2 and 3 and column 8, lines 49-51.

There is no teaching or suggestion in the combination of these references that would motivate a person of ordinary skill in the art to combine an alpha adrenergic agonist and a prostaglandin in the treatment of degeneration of the optic nerve. Although Woodward discusses the use of EP2 agonists to treat ocular nerve damage, not all such agonist compounds are themselves prostaglandins. *Yavitz* does not discuss agents other than brimonidine and Woodward does not discuss alpha adrenergic agonists.

Moreover, Woodward teaches away from the use of “prostaglandins” generally as neuroprotectants, since prostaglandin PGF2 α and other prostaglandin FP2 α receptor agonists are said to be “inactive”. The term “neuroprotection” in Woodward, as evidenced by e.g., claim 1 of the ‘211 patent, appears to be construed to exclude any neuroprotective benefits attendant to lowering IOP (and thus avoiding a mechanical crushing injury to retinal neurons). That the person of ordinary skill in the art would so adopt this interpretation is a reasonable assumption from a reading the text of Woodward, since prostaglandin F2 α , a potent ocular hypotensive, is said not to be active. ‘211 patent, column 8, lines 49-51.

Yavitz notes that the use of a single alpha adrenergic agonist, brimonidine, prior to and following LASIK surgery lessens the thinning of the retinal nerve fiber layer observed in the absence of such brimonidine use. The *Yavitz* study is not described in detail, and the reference points out that the LASIK-related nerve loss may be due to a “crushing injury” caused by raising the IOP to 80 mm Hg or greater. *Yavitz* at column 1,

¶ 3. Brimonidine is shown to mitigate this injury. However, Yavitz does not mention optic nerve degeneration or teach or even suggest the use of brimonidine to treat such injury. Indeed, the only conditions mentioned by Yavitz are retractive surgery, such as LASIK, and glaucoma. Yavitz does not disclose whether other IOP-lowering agents were used as controls to test the hypothesis that brimonidine is neuroprotective. Finally, Yavitz does not mention or even suggest the use of prostaglandins.

Each and every limitation of a claim must be either suggested or taught by the prior art in order to establish a *prima facie* case of obviousness. See e.g., MPEP § 2143.03, citing *In re Wilson*, 424 F.2d 1382, 165 USPQ 494 (CCPA 1970). Neither Yavitz nor Woodward, alone or in combination teaches or suggests a method for treating degeneration of the optic nerve, treating any condition with a combination of a prostaglandin and an alpha agonist, or teaches or suggests the generic alpha agonist structure presented in claim 21.

Applicants thus believe it is manifest that neither Yavitz nor Woodward, alone or in combination with the other, teaches, suggests, or motivates one of ordinary skill in the art to conceive of the present invention, comprising a method for the treatment of degeneration of the optic nerve comprising administering an alpha adrenergic agonist and a prostaglandin to a patient in need thereof, with a reasonable expectation of success.

For these reasons, the Applicants respectfully request that the Board of Patent Appeals and Interferences *reverse* the Examiner's holding that claim 21 is *prima facie* obvious over the combination of Yavitz and Woodward.

II. CLAIM 22

- a. Did the Examiner err in holding that Claim 22 is *prima facie* obvious over the combination of Yavitz, E., OCULAR SURG. NEWS 17:28 (September 1999) and Woodward (U.S. Patent 5,877,211) ?
 - i. *The Examiner has not met the burden of establishing a prima facie conclusion of obviousness, because nothing in the combination of the Yavitz and Woodward references motivates or suggests to one of ordinary skill in the art to combine an alpha adrenergic agonist of the specified generic structure and a prostaglandin selected from the Markush group of prostaglandins contained in claim 22 for the currently claimed purpose for the treatment of degeneration of the optic nerve.*

Claim 22 is dependent from claim 21, described above. In this claim the prostaglandin is selected from a Markush group that includes a variety of prostaglandins.

Applicants respectfully believe this claim is not *prima facie* obvious for the reasons set forth in reference to claim 21, above, and hereby incorporate the arguments herein by reference.

In addition, neither Yavitz nor Woodward, alone or in combination with the other, teaches, suggests, or motivates one of ordinary skill in the art to select a compound set forth in the Markush group of claim 22 in combination with an alpha-adrenergic component for the treatment of degeneration of the optic nerve.

Yavitz is silent with regard to conditions other than refractive surgery and glaucoma, and with regard to any compounds other than brimonidine. Woodward is drawn only to EP2 agonists as neuroprotective agents. However, Woodward does not teach, suggest or indeed provide any reason or motivation for one to combine an EP2 agonist with an alpha-adrenergic agonist.

ii. *The Examiner has not met the burden of establishing a prima facie conclusion of obviousness, because Woodward teaches away from the claimed invention.*

Woodward states that prostaglandin F2 α and its derivatives are “inactive”, and that neuroprotection is a “specific EP2 receptor mediated effect”. ‘211 patent, column 8, lines 49-51. Indeed, Woodward is really only concerned with, and only provides data concerning the EP2 agonists PGE2 and trans-2-[-4(1-hydroxyhexyl)phenyl]-5-oxocyclopentaneheptanoic acid; see ‘211 patent, paragraph bridging columns 4 and 5 and Figures 1C and 1D. Thus, Woodward teaches away from the use of prostaglandins *per se*, and from prostaglandins other than prostaglandin EP2, such as prostaglandin F2 α and its derivatives, which are all part of this Markush group. Thus, Woodward teaches away from the invention of claim 22.

III. CLAIM 23

- a. Did the Examiner err in holding that Claim 23 is *prima facie* obvious over the combination of Yavitz, E., OCULAR SURG. NEWS 17:28 (September 1999) and Woodward (U.S. Patent 5,877,211)?

- i. *The Examiner has not met the burden of establishing a prima facie conclusion of obviousness, because nothing in the combination of the Yavitz and Woodward references motivates or suggests to one of ordinary skill in the art to combine an alpha adrenergic agonist of the specified generic structure and a prostaglandin selected from the Markush group of prostaglandins contained in claim 23 for the currently claimed purpose for the treatment of degeneration of the optic nerve.*

Claim 23 is dependent from claim 22, described above. In this claim the prostaglandin is selected from a Markush group that includes a variety of prostaglandin F2 α derivatives.

Applicants respectfully believe this claim is not obvious for the reasons set forth in reference to claims 21 and 22, above, and hereby incorporate the arguments made with respect to these claims herein by reference.

In addition, neither Yavitz nor Woodward, alone or in combination with the other, teaches, suggests, or motivates one of ordinary skill in the art to select a compound comprising a prostaglandin F2 α or derivatives thereof to combine with an alpha adrenergic agonist (including brimonidine) in the treatment of degeneration of the optic nerve. Indeed, the Examiner has not alleged that the prior art does accomplish this.

- ii. *The Examiner has not met the burden of establishing a prima facie conclusion of obviousness, because Woodward teaches away from the use of compounds other than prostaglandin EP2 receptor agonists as neuroprotectants.*

Woodward states that prostaglandin F2 α and its derivatives are “inactive”, and that neuroprotection is a “specific EP2 receptor mediated effect”. ‘211 patent, column 8, lines 49-51. Indeed, Woodward is really only concerned with, and only provides data concerning the EP2 agonists PGE2 and trans-2-[-4(1-hydroxyhexyl)phenyl]-5-oxocyclopentaneheptanoic acid; see ‘211 patent, paragraph bridging columns 4 and 5 and Figures 1C and 1D. Thus, Woodward teaches away from the use of prostaglandins *per se*, and from prostaglandins other than prostaglandin EP2, such as prostaglandin F2 α and its derivatives, the only members of the “prostaglandin” Markush group of claim 23. Thus, Woodward teaches away from the invention of claim 23.

CLAIM 24

- b. Did the Examiner err in holding that Claim 24 is *prima facie* obvious over the combination of Yavitz, E., OCULAR SURG. NEWS 17:28 (September 1999) and Woodward (U.S. Patent 5,877,211)?
- i. *The Examiner has not met the burden of establishing a prima facie conclusion of obviousness, because nothing in the combination of the Yavitz and Woodward references motivates or suggests to one of ordinary skill in the art to combine an alpha adrenergic agonist of the specified generic structure contained in claim 24 with a prostaglandin for the currently claimed purpose for the treatment of degeneration of the optic nerve.*

Claim 24 is dependent from claim 21, described above. In this claim the alpha-adrenergic agonist is selected from compounds meeting the criteria set forth in the generic structure of the Markush group of claim 24.

Applicants respectfully believe this claim is not obvious for the reasons set forth in reference to claim 21 above, and hereby incorporate the arguments made with respect to these claims herein by reference.

In addition, neither Yavitz nor Woodward, alone or in combination with the other, teaches, suggests, or motivates one of ordinary skill in the art to select a compound comprising a prostaglandin F2 α or derivatives thereof to combine with brimonidine or any other alpha adrenergic agonist in the treatment of degeneration of the optic nerve. This is only the more evident given the narrower generic claim setting forth the species of alpha adrenergic compounds encompassed in the method of claim 24.

As stated above, each and every limitation of a claim must be either suggested or taught by the prior art in order to establish a *prima facie* case of obviousness. See e.g., MPEP § 2143.03, citing *In re Wilson*, 424 F.2d 1382, 165 USPQ 494 (CCPA 1970). Neither Yavitz nor Woodward, alone or in combination teaches or suggests a method for treating degeneration of the optic nerve, treating any condition with a combination of a prostaglandin and an alpha agonist, or teaches or suggests the generic alpha agonist structure present in claim 24.

IV. CLAIM 25

- a. Did the Examiner err in holding that Claim 25 is *prima facie* obvious over the combination of Yavitz, E., OCULAR SURG. NEWS 17:28 (September 1999) (hereinafter “Yavitz”) and Woodward (U.S. Patent 5,877,211) (hereinafter “Woodward”)?

- i. *The Examiner has not met the burden of establishing a prima facie conclusion of obviousness, because nothing in the combination of the Yavitz and Woodward references motivates or suggests to one of ordinary skill in the art to combine brimonidine with a prostaglandin of the structure required by claim 25 for the currently claimed purpose for the treatment of degeneration of the optic nerve.*

Claim 25 is dependent from claim 14, a cancelled claim. Applicants have filed a Rule 41.33 Amendment, which has not yet been indicated as entered, in which this error has been corrected to make this claim dependent from claim 23, described above. In this claim the alpha adrenergic agonist is further limited to brimonidine. Applicants argument are directed to the claim with its dependency corrected.

Applicants respectfully believe this claim is not obvious for the reasons set forth in reference to claims 21, 22 and 23 above, and hereby incorporate the arguments made with regarding to these claims herein by reference.

In addition, neither Yavitz nor Woodward, alone or in combination with the other, teaches, suggests, or motivates one of ordinary skill in the art to select a compound set forth in the Markush group of claim 23 in combination with brimonidine for the treatment of degeneration of the optic nerve.

Yavitz is silent with regard to the use of brimonidine for conditions other than refractive surgery and glaucoma. Woodward is drawn only to EP2 agonists as neuroprotective agents. However, Woodward does not teach, suggest or indeed provide any reason or motivation for one to combine an EP2 agonist with an alpha-adrenergic agonist generally or brimonidine in particular. The combination of Yavitz and Woodward does not lead the person of ordinary skill in the art to the method of claim 25, much less provide, as is required by law, any reasonable expectation in doing so.

V. CLAIM 27

- a. Did the Examiner err in holding that Claim 27 is *prima facie* obvious over the combination of Yavitz, E., OCULAR SURG. NEWS 17:28 (September 1999) and Woodward (U.S. Patent 5,877,211)?

- i. *The Examiner has not met the burden of establishing a prima facie conclusion of obviousness, because nothing in the combination of the Yavitz and Woodward references motivates or suggests to one of ordinary skill in the art to combine brimonidine with the 11-pivalyl ester of PGF2 α for the currently claimed purpose for the treatment of degeneration of the optic nerve.*

Claim 27 is dependent from claim 21, described above. In this claim the alpha adrenergic agonist is further limited to brimonidine and the prostaglandin to the 11-pivalyl ester of PGF2 α .

Applicants respectfully believe this claim is not obvious for the reasons set forth in reference to claims 21, 22 and 23 above, and hereby incorporate the arguments made with regard to these claims herein by reference.

In addition, neither Yavitz nor Woodward, alone or in combination with the other, teaches, suggests, or motivates one of ordinary skill in the art to select the 11-pivalyl ester of PGF2 α to combine with brimonidine for the treatment of degeneration of the optic nerve.

- ii. *The Examiner has not met the burden of establishing a prima facie conclusion of obviousness, because Woodward teaches away from the use of compounds other than prostaglandin EP2 receptor agonists as neuroprotectants.*

Woodward states that prostaglandin F2 α and its derivatives are “inactive”, and that neuroprotection is a “specific EP2 receptor mediated effect”. ‘211 patent, column 8, lines 49-51. Indeed, Woodward is really only concerned with, and only provides data concerning the EP2 agonists PGE2 and trans-2-[-4(1-hydroxyhexyl)phenyl]-5-oxocyclopentaneheptanoic acid; see ‘211 patent, paragraph bridging columns 4 and 5 and Figures 1C and 1D. Thus, Woodward teaches away from the use of prostaglandins *per*

se, and from prostaglandins other than prostaglandin EP2, such as prostaglandin F2 α and its derivatives. The sole prostaglandin required by claim 27 is the 11-pivalyl ester of PGF2 α . Woodward therefore teaches away from the invention of claim 27.

Yavitz provides no teaching whatsoever with regard to the use of prostaglandins or prostaglandin receptor agonists. Thus, Yavitz cannot make up for the deficiency of Woodward.

CONCLUSION

For the foregoing reasons Applicants respectfully request that the Board affirm the patentability of the pending claims, as amended in the Rule 42.33 Amendment filed July 7, 2006, by reversing the Examiner's holding of obviousness. Each of the claims has been argued separately, thus the claims each stand or fall independently of the other claims.

Applicants have filed herewith either a check or deposit account authorization for payment of the fee associated with the filing of this Appeal Brief. If any other fee is due, Applicants hereby authorize the Commissioner to use Deposit Account 01-0885 for the payment of such fee.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Carlos A. Fisher". The signature is fluid and cursive, with the first name "Carlos" being more prominent.

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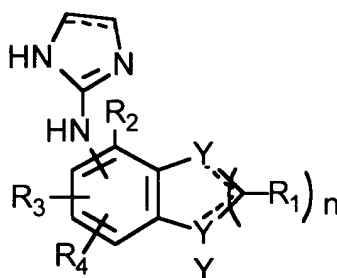
CLAIMS APPENDIX

STATUS OF CLAIMS

(not including Rule 41.33 Amendment)

1-20 (Cancelled)

21) (Previously presented) A method of treating degeneration of the optic nerve and the retinal ganglion cells of a mammal in need of such treatment, comprising administering to the mammal a therapeutically effective amount of a prostaglandin and a therapeutically effective amount of an alpha adrenergic agent of formula (I)



formula (I)

wherein each Y is independently selected from the group consisting of N, N-CH₃, O, S and C-
R₁; R₁ is hydrogen, lower alkyl or oxo; R₂, R₃ and R₄ are independently selected from the
group consisting of hydrogen, halogen, lower alkyl and lower alkenyl; n is an integer from 1 to
3; and a broken line beside a solid line indicates either a single or a double bond, provided that
two double bonds are not on the same carbon in the case when n=1, and their pharmaceutically
acceptable salts and esters as appropriate.

22. (Original) The method of claim 21 wherein the prostaglandin is selected from the group
consisting of PGF₂α, PGE₂, PGE₁, prostacyclin, 15(S)-methyl-PGF₂α, 16,16-dimethyl-

PGF2 α , 15(S)-methyl-PGE2 α , 16,16-dimethyl-PGE2, 17,18,19,20-tetranor-16-phenoxy-PGE2, 17,18, 19,20-tetranor-16-phenoxy-PGF2 α , 18,19,20-trinor-17-phenyl-PGE2, 18,19,20-trinor-17-phenyl-PGF2 α , the free acid and lower alkyl esters of PGF2 α , wherein the omega chain has been replaced with phenylethylsulfonamidomethyl-, trimoprostil, RS-84-135, rioprostil, S-1033 (15-deshydroxy PGF2 α , sodium salt), S-747260, nocloprost, CS-412, YPG-209, K-10134, cloprostenol, fluprostenol, luporstiol, etiproston, tiaprost, SQ 27986, ZK 138519, 13,14-dihydro-ZK 138519, ZK 118182, 13,14-dihydro-ZK 118182, ZK 110841, 13,14-dihydro-ZK 110841, PhXA41 (latanoprost), RO-221327, HR-466, HR-601, ONO-1206, UFO-21, 11-deoxy-PGE2, 11-deoxy-PGF2 α , 11-deoxy-16,16-dimethyl-PGE2, 11-deoxy-15(S)-methyl-PGE2, 11-deoxy-15(S)-methyl-PGF2 α , misoprostol, enisoprost, MDL-646, CL-115,574, CL-115,347, TR-4161, TR-4752, TR-4367, CP-27987, sulprostone, gemeprost, alfaprostol, delprostenate, prostalene, fenprostalene, CL-116,069, ONO-995 and RO-229648, and their pharmaceutically acceptable esters and salts, as appropriate.

23) (Original) The method of claim 22 wherein the prostaglandin is selected from the group consisting of PGF2 α -11-pivalyl ester, the 1-amido-15-methyl ether of PGF2 α , 1-ethylamido-18,19,20-trinor-17-phenyl-PGF2 α , PGF2 α -1-ethyl ester, PGF2 α -1-isopropyl ester, the acid and isopropyl ester derivatives of PGF2 α wherein the omega chain has been replaced with phenylethylsulfonamidomethyl-, as represented by the structure below:

RO-229648, SQ 27986, ZK 138519, 13,14-dihydro-ZK 138519, ZK 110841, 13,14-dihydro-ZK 110841, PhXA41, and 18,19,20-trinor-17-phenyl-PGF2 α -1-methyl ester.

24) (Original) The method of claim 21 wherein the alpha adrenergic agent is selected from the group consisting of formula (II) wherein Y is N or O, R2 is bromine or methyl and all other variables are defined as in claim 14

formula (II)

25) (Original) The method of claim 23 wherein the alpha adrenergic agent is brimonidine (5-bromo-N-(4,5-dihydro-1H-imidazol-2-yl)-6-quinoxalinamine).

26) (Cancelled)

27) (Previously presented) The method of claim 21 wherein the prostaglandin is the 11-pivalyl ester of PGF2 α and the alpha adrenergic agent is brimonidine.

EVIDENCE APPENDIX

1. Yavitz, E., OCULAR SURG. NEWS 17:28 (September 1999).
2. Woodward (US Patent 5,877,211).

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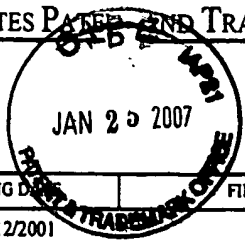
SUBSTITUTE APPEAL BRIEF
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RELATED PROCEEDINGS APPENDIX

None



UNITED STATES PATENT AND TRADEMARK OFFICE



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09/903,954	07/12/2001	Michael E. Garst	17095CIPCON(AP)	3028

7590
08/08/2006
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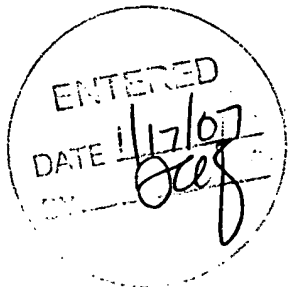
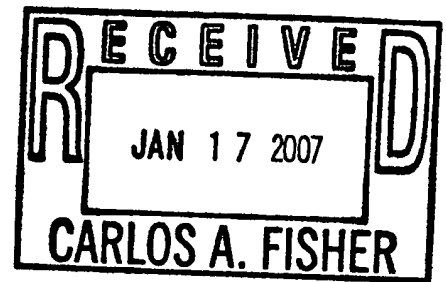
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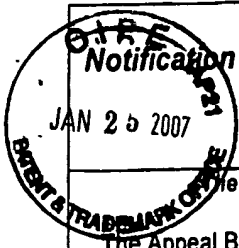
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DATE MAILED: 08/08/2006

*Response due 9/8/06
6-mo. final 2/8/07*

Please find below and/or attached an Office communication concerning this application or proceeding.





**Notification of Non-Compliant Appeal Brief
(37 CFR 41.37)**

Application No.	App' t(s)	
09/903,954	GARST, MICHAEL E.	
Examiner	Art Unit	
Zohreh Fay	1618	

The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

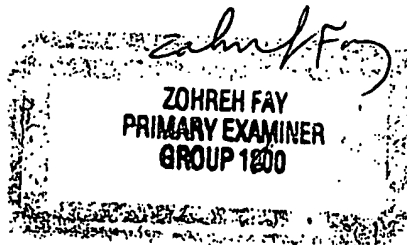
The Appeal Brief filed on 12 July 2006 is defective for failure to comply with one or more provisions of 37 CFR 41.37.

To avoid dismissal of the appeal, applicant must file an amended brief or other appropriate correction (see MPEP 1205.03) within **ONE MONTH or THIRTY DAYS** from the mailing date of this Notification, whichever is longer.

EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.136.

1. ☒ The brief does not contain the items required under 37 CFR 41.37(c), or the items are not under the proper heading or in the proper order.
2. ☐ The brief does not contain a statement of the status of all claims, (e.g., rejected, allowed, withdrawn, objected to, canceled), or does not identify the appealed claims (37 CFR 41.37(c)(1)(iii)).
3. ☐ At least one amendment has been filed subsequent to the final rejection, and the brief does not contain a statement of the status of each such amendment (37 CFR 41.37(c)(1)(iv)).
4. ☐ (a) The brief does not contain a concise explanation of the subject matter defined in each of the independent claims involved in the appeal, referring to the specification by page and line number and to the drawings, if any, by reference characters; and/or (b) the brief fails to: (1) identify, for each independent claim involved in the appeal and for each dependent claim argued separately, every means plus function and step plus function under 35 U.S.C. 112, sixth paragraph, and/or (2) set forth the structure, material, or acts described in the specification as corresponding to each claimed function with reference to the specification by page and line number, and to the drawings, if any, by reference characters (37 CFR 41.37(c)(1)(v)).
5. ☐ The brief does not contain a concise statement of each ground of rejection presented for review (37 CFR 41.37(c)(1)(vi)).
6. ☐ The brief does not present an argument under a separate heading for each ground of rejection on appeal (37 CFR 41.37(c)(1)(vii)).
7. ☐ The brief does not contain a correct copy of the appealed claims as an appendix thereto (37 CFR 41.37(c)(1)(viii)).
8. ☐ The brief does not contain copies of the evidence submitted under 37 CFR 1.130, 1.131, or 1.132 or of any other evidence entered by the examiner and relied upon by appellant in the appeal, along with a statement setting forth where in the record that evidence was entered by the examiner, as an appendix thereto (37 CFR 41.37(c)(1)(ix)).
9. ☐ The brief does not contain copies of the decisions rendered by a court or the Board in the proceeding identified in the Related Appeals and Interferences section of the brief as an appendix thereto (37 CFR 41.37(c)(1)(x)).
10. ☐ Other (including any explanation in support of the above items):

(1) Brief does not contain the heading (x) Related Proceedings Appendix. This section must have a separate heading within the brief with a note of "None" if there are no Related Proceedings.



/ Everett R. Williams/
Everett R. Williams
Patent Appeals Specialist 571-272-